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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/214,371	03/26/1999	DAVID LANE	4-20937/A/PC	8832

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EXAMINER	
ZARA, JANE J	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 05/23/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

File

Office Action Summary

Application No.	Applicant(s)
09/214,371	Lane et al
Examiner	**Art Unit**
Jane Zara	1635

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Apr 19, 2002*.

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *27-52* is/are pending in the application.

4a) Of the above, claim(s) *47-51* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *27-33, 35, 36, 38-46, and 52* is/are rejected.

7) ☒ Claim(s) *34 and 37* is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☒ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

This Office action is in response to the communication filed February 12, 2002, Paper No. 23.

Claims 27-52 are pending in the instant application.

Election/Restriction

The restriction requirement mailed April 19, 2002, Paper No. 24, is hereby vacated. This restriction requirement concerned an restriction to a single amino sequence. All sequences, however, have been rejoined and have been examined on the merits with regard to elected Group I, claims 47-51, as set forth below.

Claims 47-51 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 23.

Applicant's election with traverse of Group I in Paper No. 23 is acknowledged. The traversal is on the ground(s) that an examination on the merits of all of the groups would not present an undue burden on the examiner. This is not found persuasive because the different and distinct groups comprise I) Compositions, methods of binding inhibition and methods of purification, encompassing a vast myriad of sequences (i.e. see the generic formulae encoding SEQ ID NO: 4, 10 and 11, which include, but are not limited to SEQ ID Nos: 6, 7, 8, 12, 13 and 14); II.) Methods of inducing growth arrest or apoptosis; III.) Methods of diagnosis. A thorough

examination of each of the claimed inventions requires a very broad search of the existing prior art because of the numerous and varied sequences claimed, and furthermore the additional search of the treatment and diagnostic inventions would involve addressing additional issues such as enablement, prior art and written description. Therefore, a proper examination of all of these groups would pose an undue burden on the examiner and the searching facilities at the USPTO.

The requirement is still deemed proper and is therefore made FINAL.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 27-33, 35, 36, 38-46 and 52 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. .

The specification and claims do not indicate what distinguishing attributes are concisely shared by the members of the genus comprising compounds that bind to DM2 protein, and which comprise either the generic formula of SEQ ID NO: 4, 10 or 11. The scope of the claims includes numerous structural variants, and the genus is highly variant, because a significant number of structural differences between genus members if permitted. Concise structural features that could

distinguish compounds within the genus from others are missing from the disclosure. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general guidance, is what is needed. Since the disclosure fails to describe the common attributes or characteristics concisely identifying members of the proposed genus, and because the genus is highly variant, the description provided is insufficient. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the very broad genus claimed. Thus, Applicant was not in possession of the broad genus comprising SEQ ID Nos: 4, 10 or 11, and which polypeptides bind to DM2 protein.

Claims 27-33, 35, 36, 38-46 and 52 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for compositions comprising SEQ ID Nos: 6-8 and 12-14, methods of inhibiting DM2 binding to p53 in vitro comprising SEQ ID Nos: 6-8 and 12-14 and purification of SEQ ID Nos: 6-8 and 12-14, does not reasonably provide enablement for compositions, purification, and methods of inhibiting binding of DM2 and p53 comprising SEQ ID Nos: 4, 10 and 11, nor methods of inhibiting DM2 binding to p53 in vivo comprising SEQ ID Nos: 4, 6-8 and 10-14. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The claims are drawn to compositions, purification and methods of inhibiting DM2 binding to p53 in vitro and in vivo comprising SEQ ID Nos: 4, 6-8 and 10-14.

The following factors have been considered in determining that the specification does not enable the skilled artisan to make and/or use the invention over the scope claimed.

The state of the prior art and the predictability or unpredictability of the art. Parsons et al teach the uncertainty, absent experimentation, of the ability to attach a unique significance to a particular residue within an amino acid sequence, or of the ability to predict the biological properties of proposed amino acid sequences, including single amino acid substitutions within a polypeptide of known function (See especially page 3, first full paragraph). Parsons et al state further on page 6 that "[T]he significance of particular amino acids and sequences for different aspects of biological activity cannot be predicted *a priori* but must be determined from case to case by painstaking experimental study."

The amount of direction or guidance presented in the specification AND the presence or absence of working examples. Applicants have not provided guidance in the specification toward a method of inhibiting DM2 binding to p53 in any and/or all organisms comprising the administration of the generic compounds comprising SEQ ID Nos: 4, 10 or 11, or comprising the administration of SEQ ID Nos: 6-8, 12-14. Applicants have not provided guidance for the purification of any and or all polypeptides comprising the generic formulae of SEQ ID Nos. 4, 10 or 11. The specification teaches the inhibition of DM2 binding to p53 in vitro comprising the administration of SEQ ID Nos: 6-8, 12-14. One skilled in the art would not accept on its face the examples given in the specification of the in vitro inhibition of DM2 binding to p53 comprising the administration of SEQ ID Nos: 6-8, 12-14 as being correlative or

representative of the successful purification of any and/or all polypeptides represented by the generic formulae of SEQ ID Nos: 4, 10 or 11, nor of the ability to inhibit DM2 binding to p53 in vitro using any and/or all polypeptides represented by the generic formulae of SEQ ID Nos: 4, 10 or 11, nor of the ability to inhibit DM2 binding to p53 in vivo comprising the administration of SEQ ID Nos: 4, 6-8, 10-14, in view of the lack of guidance in the specification and known unpredictability associated with the ability to predict the biological effects exerted by any and/or all polypeptides encompassed by the generic formulae of SEQ ID Nos: 4, 10 or 11, or of the ability to predict the in vivo efficacy in their ability to inhibit the binding of DM2 to p53 comprising the administration by any means of SEQ ID Nos: 4, 6-8, 10-14. The specification as filed fails to provide particular guidance which resolves the known unpredictability in the art associated with inhibitory binding effects between DM2 and p53 in vivo using the polypeptides claimed, including those adequately described and comprising SEQ ID Nos. 6-8 and 12-14, and those inadequately described by the generic formulae comprising SEQ ID Nos: 4, 10 and 11.

The breadth of the claims and the quantity of experimentation required. The breadth of the claims is very broad. The claims are drawn to compositions, purification and methods of inhibiting DM2 binding to p53 in vitro and in vivo comprising SEQ ID Nos: 4, 6-8 and 10-14. The quantity of experimentation required to practice the invention as claimed would require the *de novo* determination of accessible target sites, modes of delivery and formulations to target appropriate cells and /or tissues in any and/or all organisms, whereby DM2 and p53 binding is inhibited in vitro and in vivo comprising the administration, by any means, of SEQ ID Nos: 4, 6-

8, 10-14. Since the specification fails to provide particular guidance for the in vivo inhibition of DM2 and p53 binding comprising administration, by any means, of SEQ ID Nos: 4, 6-8 and 10-14, and furthermore fails to adequately describe the polypeptides encompassed by the generic formulae of SEQ ID Nos: 4, 10 and 11, whereby all of the species encompassed by the broad genus are purified and their ability to prevent DM2 binding to p53 is obtained, and since determination of these factors for a particular polypeptide, or amino acid substitutions thereof, is highly unpredictable, it would require undue experimentation to practice the invention over the broad scope claimed.

Allowable Subject Matter

Claims 34 and 37 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

Certain papers related to this application may be submitted to Art Unit 1635 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone numbers for the Group are (703) 308-4242 and (703) 305-3014. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Jane Zara** whose telephone number is **(703) 306-5820.** If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader, can be reached on (703) 308-0447. Any inquiry regarding this application should be directed to the patent analyst, Katrina Turner, whose telephone number is (703) 305-3413. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

RAM SHUKLA
PRIMARY EXAMINER

JZ

May 16, 2003